Report Synopsis of Study Effect of intranasal oxytocin on social approach in patients with social phobia and healthy control

EudraCT-Nr.: 2009-015538-30

Vorlage-Nr.: 4036026

1) **Name of Sponsor/Company:** Clinical Trial Center Aachen	4) **Individual Study Table Referring to Part of the Dossier:** na[1] Volume: na Page: na	*(For National Authority Use only)*
2) **Name of Finished Product:** *Syntocinon*		
3) **Name of Active Substance:** *Oxytocin*		

5) **Title of Study[2]:** Effect of intranasal oxytocin on social approach in patients with social phobia and healthy control

Protocol version 05, 2010-01-19

no amendments

6) **Principal Investigator(s):** Univ.-Prof. Dr. med. Gerhard Gründer

7) **Study centre(s):** University Hospital RWTH Aachen, Department of Psychiatry, Psychotherapy and Psychosomatics, Pauwelsstraße 30, 52074 Aachen (single centre trial)

8) **Publication (reference):** Sarah E. Groppe, Anna Gossen, Lena Rademacher, Alexa Hahn, Luzie Westphal, Gerhard Gründer, Katja N. Spreckelmeyer (2013). Oxytocin Influences Processing of Socially Relevant Cues in the Ventral Tegmental Area of the Human Brain, Biological Psychiatry, Volume 74, Issue 3, Pages 172-179, http://dx.doi.org/10.1016/j.biopsych.2012.12.023.

Groppe, S.E., Gossen, A., Rademacher, L., Hahn, A., Westphal, L., Gründer, G. & Spreckelmeyer, K.N. (in prep.). Oxytocin normalizes dysfunctional reduction of amygdala activity during anticipation of social punishment in female social anxious patients.

9) **Studied period (years)[3]:** *Date of first enrolment: 07.06.2010* *Date of last completed: 15.12.2011* *no study suspensions or premature terminations*	10) **Phase of development:** n.a.

11) **Objectives:** The study approaches the effect of oxytocin on social interaction in social phobia using the fMRI-BOLD-response (BOLD=blood oxygen level dependent) to draw inferences of social processing and neuronal correlates and investigate an interrelation of reaction time and behavioural effects. The hormone level of the steroid hormones testosterone, progesterone und estradiole in the blood plasma are used to investigate the interaction of individul hormone levels and oxytocin action.

12) **Methodology:** Subjects with high social anxiety disorder and control subjects participated in a randomized double-blind placebo controlled repeated-measurement functional magnet-resonance imaging (fMRI) study with cross-over design. Oxytocin (26 international units) or placebo were administered via nasal spray 25 minutes before participants performed a Social Incentive Delay Task (Spreckelmeyer et al., 2009) while functional images were recorded. During the task participants are shown a cue indicating potential reward, punishment or neutral control feedback. In order to receive reward or avoid punishment (smiling or angry faces), a target button has to be pushed within a certain time window (adapted for individual reaction time). Cue-related brain activation during the anticipation phase (between cue and button press) was collected on a 3 Tesla scanner and hit rates were recorded as behavioral measure. Subjective arousal levels were assessed using self-assessment-manikin-scales. Blood samples were taken to

[1] This information is only required in connection with filing of a dossier for marketing authorization.

[2] The latest protocol version must be clearly stated, this means including all amendments – the amendments are to be declared and identified.

[3] Here also study suspensions and premature terminations of a trial/premature conclusion of a trial should be listed, including the reasons for that.

control for the hormonal state of the subjects.

13) **Number of patients (planned and analyzed):** 28 female control subjects and 12 female patients with social anxiety disorder were enrolled in the study. The planed numbers of 32 female and 32 male control subjects as well as 32 patients with social anxiety disorder could not be reached. To allow for interim analysis the study team started recruiting subjects of one gender, female subjects were included due to a better resonance of female patients with social anxiety disorder. Poor enrollment frequencies in the group of patients (just female patients were available) followed by a phase of several month without successful enrollment of social anxious subjects at all, the recruitment was suspended. No male control subjects were recruited because of the missing male patients.

14) **Diagnosis and main criteria for inclusion:**
Age between 18 and 45,

Full capacity to understand and execute instructions of the study,

For patients: diagnosis of social phobia according to ICD-10 using a minimal score of 19 in the Social Phobia Inventory (SPIN, patient assessment) and 55 points in the Liebowitz Anxiety Scale (LAS, assessment by interviewer)

exclusion criteria:

Sinistrality

Neurological or Somatic illness affecting the cerebral function (e.g. Parkinsons Disease, Epilepsy, Multiple Sclerosis, Brain Tumor)

Psychiatric disorder according to ICD-10-WHO F0-F3, F8

Psychiatric disorder according to ICD-10-WHO F (applicable in patients only in untreated or if acute occurrence in the last six months

Exclusion criteria of MRI (incorporated metal)

Positive drug test

Consumption of centrally acting substances

persons commited governmental or legaly to an institution

Additionally in women: current of former pregnancy

15) **Test product, dose and mode of administration, batch number:** Syntocinon nasal spray with a concentration of 40 I.E/ml, subjects got a dose of 26 international units (5 puffs), intranasel administration, batch numbers: OXT-fMRT/172010, OXT-fMRT/292011

16) **Duration of treatment:** Single dose administration of 26 international units Oxytocin.

17) **Reference therapy, dose and mode of administration, batch number:** Placebo nasal spray without any active substance, intranasal application, OXT-fMRT/172010, OXT-fMRT/292011

18) **Criteria for evaluation:**

Efficacy: Changes of the blood oxygen level dependent signale and the performance of the subjects during the SID task could be influenced by oxytocin, and normalised in patients..

Safety: n.a.

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19) **Statistical methods:** For fMRI-data a random-effects, event-related statistical analysis was used to look for task and treatment related changes of the blood oxygen level dependent signal. For hit rates, reaction times and hormonal levels an ANOVA on repeated measurement was performed to check for treatment related changes in the performance level. For the analysis of the fMRI-data SPM8 was used for the other data SPSS20 was used.

20) **Summary – Conclusions:**

Efficacy results:The salience of relevant social cues could be enhanced in control subjects due to a change in the blood oxygen level dependent signal in the ventral tegmental area by oxytocin. Control subjects and patients showed an enhancement of performance during the oxytocin condition, amygdala-activity could be enhanced in patients this points to an attention shift to relevant social cues. Level of oxytocin in the blood were significantly elevated after oxytocin administration, level of prolactin were reduced following oxytocin administration.

Safety results: n.a.

Conclusion: Oxytocin is a promising candiidate to help social anxious patient to refocus their attention to relevant social information and thereby enhance there perfomance in dealing with social situation. The key region in social anxious patients for this oxytocin effect seems to be the amygdala. Also control subejcts benefit from oxytocin, it seems to influence the salience of social cues but in a personality dependend manner, empathy and social competence do influence the oxytocin effect.

I hereby confirm, that the data in the results report were collected properly and are correct.

21)**Date of the report:**

Sponsor:
RTHW Aachen University, represented by the Rector,
represented by the Dean of the Medical Faculty
Univ. - Prof. Dr. rer. nat. Stefan Uhlig

Signature:

Principal Investigator:
Univ. - Prof. Dr. med. Gerhard Gründer

Signature: